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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,167	08/15/2000	Bernard Knoops	VANM143.001A	2578

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,167	KNOOPS ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/4/03; 6/13/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9 and 12-27* is/are pending in the application.

4a) Of the above claim(s) *13,15 and 17-27* is/are withdrawn from consideration.

5)☒ Claim(s) *5, 9, 12 and 16* is/are allowed.

6)☒ Claim(s) *14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 5, 9, and 12-27 are pending.

2. Claims 13, 15, and 17-27 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. In view of the amendment filed 8/4/03 and 6/13/03, the following rejections remain.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) an isolated or purified polynucleotide consisting of SEQ ID NO: 1 or its complementary strand, vector and host cell comprising said polynucleotide for in vitro diagnosis, **does not** reasonably provide enablement for *any* "pharmaceutical composition" comprising a pharmaceutical acceptable carrier and a polynucleotide consisting of SEQ ID NO: 1 or its complementary strand for treating *any* disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only (1) a human polynucleotide (cDNA) consisting of SEQ ID NO: 1 and 10, a rat polynucleotide of SEQ ID NO: 3 and a mouse polynucleotide of SEQ ID NO: 5 encoding a peroxisomal-associated polypeptides corresponding to SEQ ID NOS: 2, 4 and

6, from human, rat and mouse, respectively, (2) polynucleotide probes of SEQ ID NOS: 7-9 for in vitro diagnosis or monitoring lung injury associated with oxidative stress-related disorder.

The specification does not provide any guidance as how to treat *any* specific disease using polynucleotide mentioned above. There is insufficient guidance and lack of *in vivo* working examples using said polynucleotide for gene therapy to treat *any* disease. A "pharmaceutical composition" comprises a "polynucleotide sequence encoding a peptide for treating any diseases in the absence of *in vivo* data is unpredictable for the following reasons: (1) efficacy of the gene therapy using the polynucleotide has not been definitively demonstrated; (2) it is not always possible to extrapolate directly from in vitro diagnostic experiments to in vivo treatment of any disease; (3) the enhancing or maintaining high level expression of genes transferred to somatic cells may not persist or consistently achieved; (4) the appropriate expression of polynucleotide transfer to specific cell types (target specificity) has not been demonstrated; (5) adverse reactions from the recipient may result; (6) the lower efficiency of gene transfer (naked nucleic acid) compared with viruses and the effective therapeutic amount have not been addressed.

Das *et al* (of record) teach that getting the antisense to the cell nuclei where their anti-gene action can take place can be difficult (See abstract, in particular).

Verma *et al* (of record) teach that the problem of gene therapy is the inability to deliver genes efficiently to the right type of cell, obtaining sustained expression of the therapeutic protein and without triggering the host immune responses (See page 239, in particular). Therefore, in the absence of in vivo working examples, it would require undue experimentation of one skilled in the art to practice the claimed invention.

Given the infinite number of disease, the absence of guidance as to which specific disease that could be treated by the claimed pharmaceutical composition comprising the nucleotide of SEQ ID NO: 1 and the lack of in vivo working example demonstrating the protein encoded by the claimed polynucleotide is appropriately expressed in the appropriate tissue and in the right amount, it is unpredictable which undisclosed disease would be effectively treated by the claimed pharmaceutical composition. As such, further research would be required to practice the claimed invention. For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 2/24/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims have been amended. (2) means to deliver genetic material for therapeutic purpose were known at the time of the claimed invention. (3) the claimed composition does not need to work perfectly in order to meet the requirement of 35 USC § 112, first paragraph. (3) Applicant assert that the first example systemic administration of recombinant perosiredoxin 5 (PRDX5) to mice induced a dose-dependent neuroprotection against excitotoxic brain lesions. The eluted protein PDRX5 in PBS is an example of a pharmaceutical composition.

However, claim 14 still recites "pharmaceutical composition" comprising the polynucleotide of SEQ ID NO: 1 or its complementary strand that reads on gene therapy. There is insufficient guidance and lack of in vivo working example demonstrating that claimed pharmaceutical composition could treat any disease. There is no showing in the specification as filed that the protein encoded by the polynucleotide of SEQ ID NO: 1 or its complementary strand in the claimed pharmaceutical composition is appropriately expressed in the appropriate tissue and in the right amount, much less for treating any disease. The instant specification has no in vivo working example, let alone administering recombinant peroxiredoxin 5 (PRDX5) to mice. Even if the inventors have demonstrated that the systemic administrations of recombinant peroxiredoxin 5 (PRDX5), which is a protein or polypeptide, to mice and induced a dose-dependent neuroprotection against excitotoxic brain lesions, it is irrelevant for instant claims which drawn to polynucleotide, let alone gene therapy (pharmaceutical composition comprising a polynucleotide). Given the indefinite number of disease, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

In response to applicants' argument that the eluted protein PDRX5 in PBS is an example of a pharmaceutical composition, the claims are drawn to a pharmaceutical composition comprising a polynucleotide of SEQ ID NO: 1, and not a protein.

6. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** for *any* "pharmaceutical composition" comprising a pharmaceutical acceptable carrier and a polynucleotide consisting of SEQ ID NO: 1 or its complementary strand for treating *any* disease.

The specification discloses only (1) a human polynucleotide (cDNA) consisting of SEQ ID NO: 1 and 10, a rat polynucleotide of SEQ ID NO: 3 and a mouse polynucleotide of SEQ ID NO: 5 encoding a peroxisomal-associated polypeptides corresponding to SEQ ID NOS: 2, 4 and 6, from human, rat and mouse, respectively, (2) polynucleotide probes of SEQ ID NOS: 7-9 for in vitro diagnosis or monitoring lung injury associated with oxidative stress-related disorder.

There is inadequate written description about the disease to be treated by the claimed pharmaceutical composition comprising a polynucleotide consisting of" SEQ ID NO: 1 or its complementary strand given the indefinite number of disease, not to mentioned the lack of working examples. Further, the specification merely states a pharmaceutical composition comprising a polynucleotide of SEQ ID NO: 1. Given the infinite number of disease, the pharmaceutical composition that read on gene therapy is not adequately described. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *see University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 8/4/03 have been fully considered but are not found persuasive.

Applicants' position is that claims 5 and 14 have been amended and claim 32 has been canceled.

However, claim 14 still recites "pharmaceutical composition" comprising the polynucleotide of SEQ ID NO: 1 or its complementary strand that reads on gene therapy. There is insufficient written description about the specific disease to be treated by the claimed pharmaceutical. Further, there is no showing in the specification as filed that the protein encoded by the polynucleotide of SEQ ID NO: 1 or its complementary strand in the claimed pharmaceutical composition is appropriately expressed in the appropriate tissue and in the right amount, much less for treating any disease. The instant specification has no in vivo working example, let alone administering recombinant peroxiredoxin 5 (PRDX5) to mice. Even if the inventors have demonstrated that the systemic administrations of recombinant peroxiredoxin 5 (PRDX5), which is a protein or polypeptide, to mice and induced a dose-dependent neuroprotection against excitotoxic brain lesions, it is irrelevant for instant claims which drawn to polynucleotide. The claimed pharmaceutical composition comprising the polynucleotide of SEQ ID NO: 1 reads on gene therapy for treating any disease. Given the indefinite number of disease, the pharmaceutical composition is not adequately described.

7. The following new ground of objection is necessitated by the amendment filed 8/4/03 and 6/13/03.

8. The disclosure is objected to because the Brief description of the drawings for Figure 5 is no longer match with the formal drawing filed 6/13/03. Specifically, "Figure 5" in Brief description of Drawings should have been "Figure 5A-C" to match with the amended drawings. Further, SEQ ID NO: is required for the B18 mouse sequence.

9. Claims 5, 9, 12, and 16 are allowed.

10. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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October 20, 2003

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